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CHILD Syndrome in a Boy

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CHILD syndrome (congenital hemidysplasia with ichthyosiform nevus and limb defects) occurs, as a rule, exclusively in girls because the underlying X-linked gene exerts a lethal effect on male embryos. In this report the characteristic manifestations of CHILD syndrome are described in a 2-year-old boy with a normal chromosome constitution 46,XY. This exceptional case is best explained by the assumption of an early somatic mutation and thus compatible with the concept of X-linked dominant male-lethal inheritance of this trait.

KEY WORDS: CHILD syndrome, X-linked dominant, male-lethal inheritance, lateralization pattern, lines of Blaschko, postzygotic mutation, gametic half-chromatid mutation

INTRODUCTION

The term CHILD syndrome is an acronymic designation that stands for congenital hemidysplasia with ichthyosiform nevus and limb defects [Happle, 1990]. The condition is virtually always observed in girls because the underlying X-linked dominant gene exerts a lethal effect on male embryos [Happle et al., 1980]. As an exception to this rule we here report the occurrence of CHILD syndrome in a boy.

CLINICAL REPORT

The 2-year-old boy was the first child of healthy nonconsanguineous parents of Egyptian origin. At birth, a severely deformed right leg and an inflammatory ichthyosiform skin lesion involving the right side of the body were noted.

On physical examination, an inflammatory nevus showing yellow, waxy scaling involved the right half of the trunk, with a sharp demarcation on the dorsal and ventral midline (Fig. 1). The nevus diffusely involved the abdomen but showed a linear arrangement, following the lines of Blaschko, on the upper part of the thorax and the right arm (Fig. 2). On the right buttock and the dorsal aspect of the right thigh a linear area of unaffected skin was noted. The right lower leg was short and showed lack of the fibula as well as malposition and severe hypoplasia of the foot (Figs. 3, 4). Further examination did not show any involvement of other organs such as the eyes, brain, heart, or kidneys.

Histopathological examination of a biopsy obtained from lesional skin of the abdomen showed acanthosis and marked parakeratosis (Fig. 5) intermingled with areas of orthohyperkeratosis and lymphohistiocytic infiltrates involving the upper part of the dermis. Considerable numbers of neutrophils were present in the epidermis. In the stratum corneum they tended to form accumulations reminiscent of Munro abscesses. The dermal papillae were filled with histiocytes showing a foamy cytoplasm resulting in a characteristic histopathological pattern of "verruciform xanthoma" (Fig. 6) [Happle, 1991]. With Sudan staining the foamy structures were identified as lipids.

Cytogenetic analysis of peripheral blood lymphocytes showed a normal male karyotype 46,XY.

As a tentative treatment for the CHILD nevus, dermabrasion of parts of the lesion involving the trunk was performed under general anesthesia. Two weeks after this operation the treated skin looked much better, but 8 months later the CHILD nevus had completely recurred in the treated area. In the meantime, the boy had undergone orthopedic surgical correction of the dislocation of his right knee joint and his right foot, resulting in some functional improvement.

DISCUSSION

The occurrence of CHILD syndrome in a boy with a normal XY constitution is unusual but does not invalidate the concept of X-linked dominant inheritance with lethality for male embryos. Almost all cases so far reported have been observed in girls [Happle, 1990; Peter and Meinecke, 1993], and transmission from mother to daughter has been described [Happle et al., 1990]. Remarkably, the first published case that can retrospec-

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Fig. 1. The patient showing striking lateralization of the skin lesions.

Fig. 2. CHILD nevus showing linear arrangement on the thorax and the right arm.

Fig. 3. Shortening of the right lower leg with marked hypoplasia and malposition of the foot.

tively be classified as CHILD syndrome was a boy [Zellweger and Uehlinger, 1948].

It is well known that other X-linked dominant, male-lethal traits such as incontinentia pigmenti, focal dermal hypoplasia, or oral-facial-digital (OFD I) syndrome may exceptionally occur in males [Wettke-Schäfer and Kantner, 1983]. In some of these cases a karyotype 47,XXY has been documented [Wahrman et al., 1966; Kunze et al., 1977; García-Dorado et al., 1990], but the remaining patients had a normal karyotype 46,XY

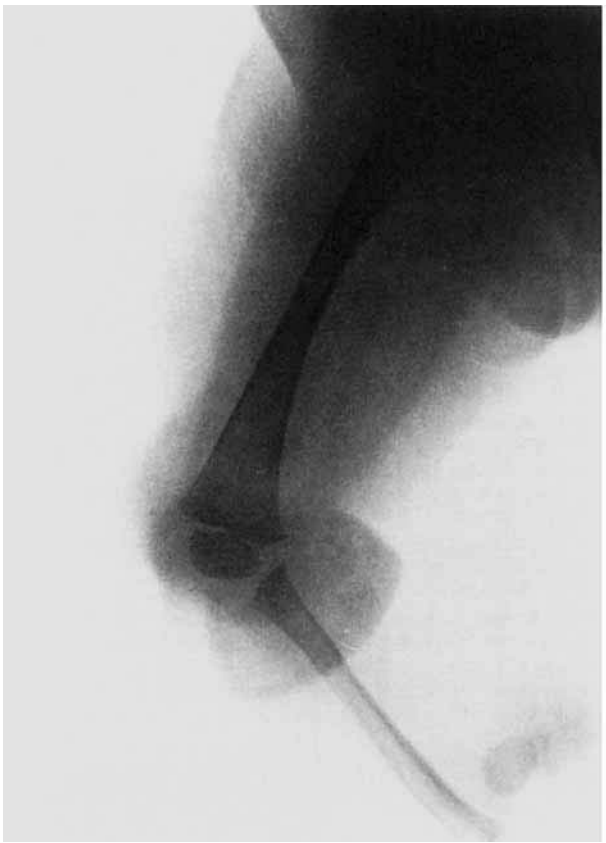

Fig. 4. X-ray of the right leg showing absence of the fibula.

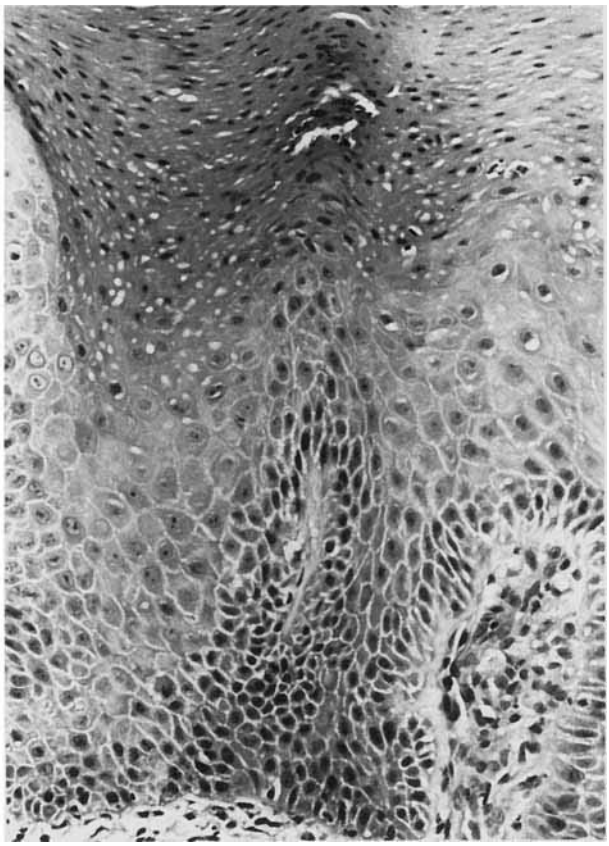

Fig. 5. Biopsy obtained from CHILD nevus showing acanthosis and marked parakeratosis characterized by corneocytes with conserved nuclei (uppermost part of photograph) (hematoxylin and eosin, ×100).

Fig. 6. Subcorneal accumulation of neutrophils (large arrow) and enlarged dermal papillae filled with foamy histiocytes (small arrow) (hematoxylin and eosin, ×160).

[Pallisgaard, 1969; Burgdorf et al., 1981; Sommer and Liu, 1984]. Such cases can be best explained either by a postzygotic mutation or by a gametic half-chromatid mutation [Lenz, 1975]. The present case is apparently likewise caused by one of these mechanisms. In view of the pattern of lateralization of the lesions, the action of a postzygotic mutation appears more likely than the assumption of a gametic half-chromatid mutation that should be expected to give rise to a more finely distributed, bilateral pattern.

According to this concept, XY men affected with CHILD syndrome can transmit the trait to their daughters, provided the underlying postzygotic mutation has occurred rather early and involves the gonads, too. Conversely, a transmission of this phenotype from mother to son is not possible. In apparent contrast with this idea, 2 cases of an alleged transmission of incontinentia pigmenti from mother to son have been reported [Hecht et al., 1982; Kurczynski et al., 1982]. However, the clinical documentation of these cases is too vague to draw firm conclusions, and the auxiliary hypotheses of an unstable forward-backward mutation [Langenbeck, 1982] or of an unstable premutation [Traupe and Vehring, 1994] seem unnecessary.

In conclusion, the occurrence of CHILD syndrome in a boy with a normal karyotype 46,XY is uncommon but compatible with the concept of an X-linked dominant, male-lethal mutation. For the practical purpose of genetic counseling it should be borne in mind that a man affected with CHILD syndrome bears a risk to transmit the trait to his daughters.

REFERENCES

Burgdorf WHC, Dick GF, Soderberg HD, Goltz RW (1981): Focal dermal hypoplasia in a father and daughter. J Am Acad Dermatol 4:273–277.

García-Dorado J, De Unamuno P, Fernández-López E, Salazar Veloz J, Armijo M (1990): Incontinentia pigmenti: XXY male with a family history. Clin Genet 38:128–138.

Happle R (1990): Ptychotropism as a cutaneous feature of the CHILD syndrome. J Am Acad Dermatol 23:763–766.

Happle R (1991): CHILD naevus is not ILVEN. J Med Genet 28:214.

Happle R, Karlic D, Steijlen PM (1990): CHILD-Syndrom bei Mutter und Tochter. Hautarzt 41:105–108.

Happle R, Koch H, Lenz W (1980): The CHILD syndrome: Congenital hemidysplasia with ichthyosiform erythroderma and limb defects. Eur J Pediatr 134:27–33.

Hecht F, Hecht BK, Austin WJ (1982): Incontinentia pigmenti in Arizona Indians including transmission from mother to son inconsistent with the half chromatid mutation model. Clin Genet 21: 293–296.

Kunze S, Frenzel UH, Hüttig E, Grosse FR, Wiedemann HR, Happle R (1977): Klinefelter's syndrome and incontinentia pigmenti Bloch-Sulzberger. Hum Genet 35:237–240.

Kurczynski TW, Berns JS, Johnson WE (1982): Studies of a family with incontinentia pigmenti variably expressed in both sexes. J Med Genet 19:447–451.

Langenbeck U (1982): Transmission of incontinentia pigmenti from mother to son is consistent with a half chromatid back-mutation (reversion) model. Clin Genet 22:290–291.

Lenz W (1975): Half chromatid mutations may explain incontinentia pigmenti in males. Am J Hum Genet 27:690.

Pallisgaard G (1969): Incontinentia pigmenti in a newborn boy. Acta Derm Venereol (Stockh) 49:197–201.

Peter C, Meinecke P (1993): CHILD-Syndrom: Fallbericht einer seltenen Genodermatose. Hautarzt 44:590–593.

Sommer A, Liu PH (1984): Incontinentia pigmenti in a father and his daughter. Am J Med Genet 17:655–659.

Traupe H, Vehring KH (1994): Unstable premutation may explain mosaic disease expression of incontinentia pigmenti in males. Am J Med Genet 49:397–398.

Wahrman J, Berant M, Jacobs J, Aviad I, Ben-Hur N (1966): The oral-facial-digital syndrome: A male-lethal condition in a boy with 47-XXY chromosomes. Pediatrics 37:812–821.

Wettke-Schafer R, Kantner G (1983): X-linked dominant inherited diseases with lethality in hemizygous males. Hum Genet 64:1–23.

Zellweger H, Uehlinger E (1948): Ein Fall von halbseitiger Knochenchondromatose (Ollier) mit Naevus ichthyosiformis. Helvet Paediatr Acta 2:153–163.